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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,021	06/24/2003	Himanshu Brahmbhatt	060348-0104	7643
22428 7590 07/25/2008 FOLEY AND LARDNER LLP SUITE 500 3000 K STREET NW WASHINGTON, DC 20007				
EXAMINER				
LANKFORD JR, LEON B				
ART UNIT		PAPER NUMBER		
1651				
MAIL DATE		DELIVERY MODE		
07/25/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/602,021

**Applicant(s)**

BRAHMBHATT ET AL.

**Examiner**

Leon B. Lankford

**Art Unit**

1651

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 3/10/2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 9, 11, 12 and 27-44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9, 11, 12 and 27-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)
- Paper No(s)/Mail Date \_\_\_\_\_

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/10/2008 has been entered. The declaration of 3/10/2008 has been fully considered as well.

In the interview of March 3, 2008 it was stressed to the examiner the significance of applicant's finding that minicells have a uniform diameter of 0.4 microns and it was that elucidation that led to the claimed invention. A reexamination of the prior art however (as discussed in detail below) shows that a .45 micron filter was previously used to isolate minicells from vegetative cells.

Applicant states in the declaration that: "The use of filtration requires knowledge of the size and uniformity of the particles to be purified. Neither of these prerequisites was known prior to our invention." Applicant also states "conventional wisdom held that filtration would not be useful for purifying bacterial minicells."

However, in the instant case since one of ordinary skill in the art would recognize the size of the filamentous bacteria and know that the minicells were smaller,

would could choose a proper filter based purely in that information. It is not consistent with the purview of one of ordinary skill in the art at the time the invention was made to say that filtration is not a suitable means for size-based separation. Given the purview of said one of ordinary skill in the art it would have been obvious at the time the invention was made to use filtration to exclude (trap) filamentous bacteria and allow minicells to pass into a filtrate. Furthermore, applicant had previously cited prior art, Christen et al *Gene* 23, in which *E coli* minicells were separated from bacterial vegetative cells utilizing glass fiber filters having a pore size of 0.45 or 0.65 microns. Further in applicant's own specification, paragraph [013], applicant recognizes that filtration has been used for the isolation of minicells. Applicant's preferred filter would appear to be the same .45 micron filter used successfully by Christen, so it is unclear how this could be considered unobvious.

The previous filtrations (a size separation technique) discussed in the prior art did not utilize a step where the "contaminating" bacteria were induced to form filaments, however Khatchatourians induced filamentation of normal, contaminating cells in concentrated minicell preparations, followed by selective elimination of the contaminating cells and ultimately obtained high yields of minicells by centrifugation (a size separation technique).

Applicant is directed to pages 12-13 of *KSR v Teleflex* (500 US \_\_\_\_ 2007) " ... the Court has held that a "patent for a combination which only unites old elements with no

change in their respective functions . . . obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men.”

Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U. S. 147, 152 (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” “When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either *in the same field or a different one(emphasis added)*. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.”

In the instant case, the prior art as a whole teaches that one should use any means known and necessary to eliminate the vegetative cells from the minicells in a desired minicell prep- typically and ultimately using the size differential of the minicell and the undesired contaminants to purify the minicells. As such the claimed invention was obvious at the time the invention was made.

Applicant has suggested that Khatchatourians is flawed because sonication will lyse minicells as well as normal cells. This argument is intriguing, however, it should be noted that the reference did report the isolation of intact minicells and as such “discrediting” this piece of prior art would require more empirical data. An analysis of

the type and intensity of the sonication used versus what the prior art suggest for lysing the minicells may be helpful.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 11-12 and 27-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing in that the independent claim 9 offers as a critical element that the minicells are 0.4 microns in diameter yet the dependent claims use filters with pores of 0.45 or greater or less than 0.2 thus questioning the criticality of the 0.4. The limitation of 0.2 would seem to conflict directly with claim 9. It is noted that a reading of the specification would suggest that applicant intends the 0.2 pore filter to be used in a subsequent step however the claims do not clearly recite that.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 9, 11-12 and 27-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khatchatourians et al (BIOCHEMISTRY 3(3) 1973) in view of Christen et al(*Gene* 23).

Khatchatourians teaches the separation of minicells from normal, contaminating bacterial cells by inducing the normal cells to filamentate followed by selective elimination of the filamentous bacteria (page 297):

"We...induced filamentation of normal, contaminating cells in concentrated minicell preparations, followed by selective elimination of the contaminating cells. We were able to obtain high yields of minicells..."

The reference does not use the claimed method for inducing filamentation or the filtering method to remove the filamentous bacteria from the minicells however at the time the invention was made it would have been considered obvious given the teachings of Khatchatourians to use any well known method to induce the formation of filamentous bacteria (stress induction is old and well known) and then use any obvious "selective elimination" to separate the two physically distinct cell types remaining in the sample, i.e. minicells and filamentous bacteria. Given the state of the art at the time applicant's invention was made, it would have been obvious that one could have separated the filamentous bacteria from the minicells using available filters with micrometer pore sizes which would allow the passage of minicells while holding the

filamentous bacteria thus achieving Khachatourins' "selective elimination" of the normal bacteria. Christen et al teach that such could be accomplished by using .45 or 0.65 micron filters.

One of ordinary skill in the art would recognize the size of the filamentous bacteria and know that the minicells were smaller, would could choose a proper filter based purely in that information. Given the purview of said one of ordinary skill in the art it would have been obvious at the time the invention was made to use filtration to exclude (trap) filamentous bacteria and allow minicells to pass into a filtrate particularly in view of Christen et al in which *E coli* minicells were separated from bacterial vegetative cells utilizing glass fiber filters having a pore size of 0.45 or 0.65 microns. The previous filtrations (a size separation technique) discussed in the prior art did not utilize a step where the "contaminating" bacteria were induced to form filaments, however Khachatourians induced filamentation of normal, contaminating cells in concentrated minicell preparations, followed by selective elimination of the contaminating cells and ultimately obtained high yields of minicells by centrifugation (a size separation technique). Knowing that minicells could be separated from other cells (and of course other contaminants) using one size separation technique, it would have been obvious to use other known methods for size separation (a finite group) with the predictable result that the minicells would be separated.

Applicant is directed to pages 12-13 of *KSR v Teleflex* (500 US \_\_\_\_ 2007) " ... the Court has held that a "patent for a combination which only unites old elements with no



change in their respective functions . . . obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men.”

Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U. S. 147, 152 (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” “When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either *in the same field or a different one(emphasis added)*. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.”

In the instant case, the prior art as a whole teaches that one should use any means known and necessary to eliminate the vegetative cells from the minicells in a desired minicell prep- typically and ultimately using the size differential of the minicell and the undesired contaminants to purify the minicells. As such the claimed invention was obvious at the time the invention was made.

Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon B. Lankford whose telephone number is 571-272-0917. The examiner can normally be reached on Mon-Thu 7:30-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/  
Primary Examiner, Art Unit 1651